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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,873	12/06/2004	Hilmar Meek Warenius	376956-002US	1109

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EXAMINER	
HALVORSON, MARK	
ART UNIT	**PAPER NUMBER**
1642	
MAIL DATE	**DELIVERY MODE**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,873	WARENIUS ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 2/26/2007.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 and 18-28 is/are pending in the application.

4a) Of the above claim(s) 6, 9-15, 18-28 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5, 7 and 8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15, 18-28 are pending.

Claim 6, 9-15, 18-28 have been withdrawn.

Claims 1-5, 7 and 8 are under currently under examination.

35 USC § 102(b) rejections withdrawn

The rejection of claims 1, 2, 7 and 8 under 35 U.S.C. 102(b) as being anticipated by Kelly et al is withdrawn in view of Applicants amendments.

35 USC § 103(a) rejections withdrawn

The rejection of claims 3–5 under 35 U.S.C. 103(a) as being unpatentable over Kelly et al as applied to claims 1 and 2, above, and further in view of Theryte Limited is withdrawn in view of Applicants amendment.

NEW REJECTIONS: Based on the Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hybridon (WO 99/27087, published June 3, 1999).

Claims 1, 2, and 7 are drawn to a method of screening for an agent effective in the treatment of a cancer, which method comprises selecting a putative agent that is likely to disrupt a non-kinase function mediated by CDK4 and treating a cancer cell sample and a control cell sample with the putative agent, and determining growth

inhibiting effect of the putative agent on these samples and identifying an effective agent as an agent which is more inhibiting to the growth of the cancer cell sample than the control cell sample.

Hybridon discloses antisense molecules that bind to the CDK4 gene and inhibit the expression of CDK4 (page 15 line 1 to page 17 line 28) . Hybridon further discloses that other antisense molecules that inhibit CDK4 expression can be identified (page 17 line 30 to page 18 line3). The antisense molecules can be used for treating a mammal afflicted with a tumor associated with the aberrant expression of CDK4 (Abstract). An antisense molecule would suppress expression of the CDK protein and would disrupt the non-kinase function mediated by CDK4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2 and 7 rejected under 35 U.S.C. 103(a) as being unpatentable over Beach et al (US Patent No: 5,962,316, issued October 5, 1999) in view of Haas et al (Oncogene, 1997, 15:179-192).

Claims 1, 2, and 7 are drawn to a method of screening for an agent effective in the treatment of a cancer, which method comprises selecting a putative agent that is

likely to disrupt a non-kinase function mediated by CDK4 and treating a cancer cell sample and a control cell sample with the putative agent, and determining growth inhibiting effect of the putative agent on these samples and identifying an effective agent as an agent which is more inhibiting to the growth of the cancer cell sample than the control cell sample.

Beach et al disclose a method for generating peptide or non-peptide agents based on the structure of a 16 kDa cell-cycle regulatory protein (CCR) that are able compete for binding with CDK4. (column 30 lines 16-21). Beach et al further disclose the identification of potential peptidyl fragments of CDK4 that can competitively bind to the 16 kDa CCR and interfere with its ability to bind to CDK4 (column 30 lines 58-63). The 16 kDa CCR protein disclosed in Beach et al (SEQ ID NO:2) is cyclin-dependent kinase inhibitor inhibitor 2A ($p16^{INK4a}$) (see search results from NCBI).

Beach does not disclose that the inhibition of the binding of $p16^{INK4a}$ to CDK4 would disrupt a non-kinase function mediated by CDK4).

Haas et al discloses that a catalytically inactive CDK4, that can still bind to $p16^{INK4a}$, cooperates with activated H-ras in transforming cells (page 188, 2nd column). Furthermore, CDK4 mutants that can not bind to $p16^{INK4a}$, but are still catalytically active, can no longer transform cells. (Id). Thus, binding of CDK4 with $p16^{INK4a}$ and not the kinase activity of CDK4 is critical for transforming cells with CDK4. Inhibitors that abrogate the binding of CDK4 with $p16^{INK4a}$ would disrupt a non-kinase function mediated by CDK4.

One of ordinary skill in the art would have been motivated to apply Haas et al's teaching that the binding of CDK4 with $p16^{INK4a}$ is important for cell transformation with Beach et al's method of identifying agents that inhibit binding of CDK4 with $p16^{INK4a}$ because both Haas et al (Abstract) and Beach et al (column 11, lines 8-11) disclose the importance of the CDK4 - $p16^{INK4a}$ interaction in cell transformation. It would have been prima facie obvious to combine Beach et al's method with Haas et al' s teaching to identify agents that disrupt a non-kinase function mediated by CDK4.

Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beach et al in view of Haas et al as applied to claims 1 and 2, above, and further in view of Theryte Limited (WO 99/42821, publication date 26 August 1999).

Claims 3-5 are drawn to a method of screening for an agent effective in the treatment of a cancer, which method comprises selecting a putative agent that is likely to disrupt a non-kinase function mediated by CDK4 and treating a cancer cell sample and a control cell sample with the putative agent, and determining growth inhibiting effect of the putative agent on these samples and identifying an effective agent as an agent which is more inhibiting to the growth of the cancer cell sample than the control cell sample, wherein the cancer cell sample consists of cancer cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6, wherein the cancer cell sample consists of cells in which the CDK1 and CDK4 gene products are both elevated as compared with control cells, and wherein the step of identifying an effective agent further involves determination of the ratio of the levels of the CDK1 and CDK4 gene products in the cancer cell sample before and after treatment with the putative agent.

Beach et al and Haas et al have been described supra.

Neither Beach et al nor Haas et al disclose a cancer cell sample that consists of cells in which the CDK1 and CDK4 gene products are both elevated as compared with control cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6.

Theryte discloses that CDK1 and CDK4 proteins are elevated in cancer cells (Figs. 3 and 4) and that the ration of CDK4 to CDK1 is approximately 1 (Fig 5).

One of ordinary skill in the art would have been motivated to apply Theryte's teaching of the diagnostic value of CDK1 and CDK4 levels in cancer to Haas et al and Beach et al's drug screen method because Theryte states that the increased levels of CDK1 and CDK4 in cancers may be used in drug screening that might lead to more specifically toxic to cancer tissues (page 3, 3rd paragraph). Thus, it would have been prima facie obvious to combine Haas et al and Beach et al's method for detecting CDK4 inhibitors with Theryte's finding of elevated levels of CDK4 and CDK1 in cancer.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beach et al in view of Haas et al as applied to claims 1 and 2, above, and further in view of Ceha et al (Biochem Biophys Res Comm, 1998, 249:550-555).

Claim 8 is drawn to a method of screening for an agent effective in the treatment of a cancer, which method comprises selecting a putative agent that is likely to disrupt a non-kinase function mediated by CDK4 and treating a cancer cell sample and a control cell sample with the putative agent, and determining growth inhibiting effect of the putative agent on these samples and identifying an effective agent as an agent which is more inhibiting to the growth of the cancer cell sample than the control cell sample, wherein the region of the human CDK4 gene product mediating the function required for the successful division and continued cell survival is a region between amino acids 172-285.

Beach et al and Haas et al have been described supra.

Neither Beach et al nor Haas et al disclose that the region of the human CDK4 gene product mediating the function required for the successful division and continued cell survival is a region between amino acids 172-285.

Ceha et al disclose that amino acids 209-211 and 281-283 of CDK4 are involved in the binding of binding of $p16^{INK4a}$ to CDK4

One of ordinary skill in the art would have been motivated to apply Ceha et al's teaching of the amino acids involved in the binding of $p16^{INK4a}$ to CDK4 to Haas et al and Beach et al's drug screen method to identify the regions of CDK4 that are important in the binding of $p16^{INK4a}$ to CDK4 . Thus, it would have been prima facie obvious to combine Haas et al and Beach et al with Ceha et al to identify agents that can disrupt the binding of $p16^{INK4a}$ to CDK4.

Summary

Claims 1-5, 7 and 8 stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at (571) 272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
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PRIMARY EXAMINER